Considered 08/21/03 MSC

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=> d que l23
L20           1 SEA FILE=REGISTRY ABB=ON  PLU=ON  PEG/CN
L21         298 SEA FILE=HCAPLUS ABB=ON  PLU=ON  (L20 OR PEG OR POLYETHYLENE
                GLYCOL)(L)LINKER?
L22         117 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L21 AND (BIOCONJUGAT? OR
                CONJUGAT?)
L23          35 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L22 AND (SURFACE OR SOLID OR
                SILICON OR SIO2 OR QUARTZ OR SILICA OR AU OR GOLD)


=> d ibib abs l23 1-35

L23  ANSWER 1 OF 35  HCAPLUS  COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER:         2003:413972  HCAPLUS
DOCUMENT NUMBER:          139:3252
TITLE:                    Solid-phase immobilization of proteins and
                          peptides
INVENTOR(S):              Kurz, Markus
PATENT ASSIGNEE(S):       USA
SOURCE:                   U.S. Pat. Appl. Publ., 13 pp.
                          CODEN: USXXCO
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:

     PATENT NO.        KIND  DATE          APPLICATION NO.  DATE
     ----------------  ----  --------      ---------------  --------
     US 2003100004     A1    20030529      US 2002-302456   20021121
     WO 2003045975     A2    20030605      WO 2002-US37743  20021121
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
             CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
             GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
             LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,
             PL, PT, RO, RU, SC, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT,
             TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ,
             MD, RU, TJ, TM
         RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG,
             CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL,
             PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR,
             NE, SN, TD, TG
PRIORITY APPLN. INFO.:                    US 2001-333470P  P  20011127
AB   Disclosed herein are methods for immobilizing a peptide or protein on a
     solid support.  The method generally includes the following steps:
     (a) providing one or more templates attached to a solid support,
     wherein the one or more templates include (i) an RNA encoding a peptide
     and (ii) a peptide acceptor-linker linked to the RNA; and (b) subjecting
     the one or more templates to conditions that support translation and
     attachment of said peptide to said peptide acceptor, thereby synthesizing
     the one or more peptides on the solid support.  Also disclosed
     herein are solid supports having at least one RNA-protein fusion
     component immobilized thereon, methods for generating protein arrays, and
     methods for screening mols. using these arrays.  Peptide
     MVSDVPRDLEVVAATPTSLLISWKTHEVAARYYRITYGETGGNSPVQEFTVPPW
     ASIATISGLKPGVDYTITVYAVTPLRWTETEAHIPIPINYRT was prepd. from biotinylated
     RNA on neutravidin agarose beads or streptavidin membrane.
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L23 ANSWER 2 OF 35 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2003:154922 HCAPLUS
DOCUMENT NUMBER: 138:210308
TITLE: Multicomponent assemblies having enhanced binding properties for diagnosis and therapy
INVENTOR(S): Cantrell, Gary L.; Burleigh, B. Daniel
PATENT ASSIGNEE(S): Mallinckrodt Inc., USA
SOURCE: U.S. Pat. Appl. Publ., 15 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2003039683	A1	20030227	US 2001-932291	20010817
WO 2003015606	A2	20030227	WO 2002-US25582	20020813

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2001-932291 A 20010817

AB An organized mobile multicomponent **conjugate** (OMMC) and method of using to enhance binding of weakly binding compds. to a target is described. A lamellar structure contg. at least two binding compds. is assembled under conditions in which the binding compds. self-regulate in or on the lamellar structure, forming a cooperative ensemble that is capable of binding with enhanced affinity to a complementary affinity site on a target. Each binding compd. is bound to the lamellar **surface**, and may be connected by a **linker**. The OMMC may contain an effector mol., such as a diagnostic or therapeutic agent, for administration to a patent who is then diagnosed or treated using the effector mol. For example, OMMC assemblies having one domain and a terminal carboxylate binding region, and contg. gas, i.e., docosanoate, octacosanoate, and succinylated **PEG**(100)stearate formulated with n-perfluorobutane, were prepd. as an echogenic compn. Binding of the assemblies to human umbilical cord endothelial cells was blocked by heparin or hyaluronic acid oligosaccharides, likely due to their competing for complementary affinity sites on the cell membrane or extracellular matrix.

L23 ANSWER 3 OF 35 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2003:114670 HCAPLUS
TITLE: Simple test system for single molecule recognition force microscopy
AUTHOR(S): Riener, Christian K.; Stroh, Cordula M.; Ebner, Andreas; Klampfl, Christian; Gall, Alex A.; Romanin, Christoph; Lyubchenko, Yuri L.; Hinterdorfer, Peter;

Gruber, Hermann J.
CORPORATE SOURCE: Institute of Biophysics, J. Kepler University, Linz, A-4040, Austria
SOURCE: Analytica Chimica Acta (2003), 479(1), 59-75
CODEN: ACACAM; ISSN: 0003-2670
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB We have established an easy-to-use test system for detecting receptor-ligand interactions on the single mol. level using at. force microscopy (AFM). For this, avidin-biotin, probably the best characterized receptor-ligand pair, was chosen. AFM sensors were prepd. contg. tethered biotin mols. at sufficiently low **surface** concns. appropriate for single mol. studies. A biotin tether, consisting of a 6 nm poly(ethylene glycol) (**PEG**) chain and a functional succinimide group at the other end, was newly synthesized and covalently coupled to amine-functionalized AFM tips. In particular, PEG800 diamine was glutarylated, the mono-adduct NH2-**PEG**-COOH was isolated by ion exchange chromatog. and reacted with biotin succinimidyl ester to give biotin-**PEG**-COOH which was then activated as N-hydroxysuccinimide (NHS) ester to give the biotin-**PEG**-NHS **conjugate** which was coupled to the aminofunctionalized AFM tip. The motional freedom provided by **PEG** allows for free rotation of the biotin mol. on the AFM sensor and for specific binding to avidin which had been adsorbed to mica **surfaces** via electrostatic interactions. Specific avidin-biotin recognition events were discriminated from nonspecific tip-mica adhesion by their typical unbinding force (.apprx.40 pN at 1.4 nN/s loading rate), unbinding length (<13 nm), the characteristic nonlinear force-distance relation of the **PEG linker**, and by specific block with excess of free d-biotin. The convenience of the test system allowed to evaluate, and compare, different methods and conditions of tip aminofunctionalization with respect to specific binding and nonspecific adhesion. It is concluded that this system is well suited as calibration or start-up kit for single mol. recognition force microscopy.

REFERENCE COUNT: 41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L23 ANSWER 4 OF 35 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2003:58701 HCAPLUS
DOCUMENT NUMBER: 138:119557
TITLE: Peptidomimetic protein-binding microarrays on mirrored substrates for performing proteomic analyses
INVENTOR(S): Charych, Deborah; Beausoleil, Eric; Zuckermann, Ronald N.
PATENT ASSIGNEE(S): Chiron Corporation, USA
SOURCE: U.S. Pat. Appl. Publ., 32 pp., Cont.-in-part of U.S. Pat. Appl. 2002 55,125.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2003017508	A1	20030123	US 2002-190308	20020703

US 2002055125 A1 20020509 US 2001-874091 20010604
PRIORITY APPLN. INFO.: US 2000-209711P P 20000605
US 2001-874091 A2 20010604

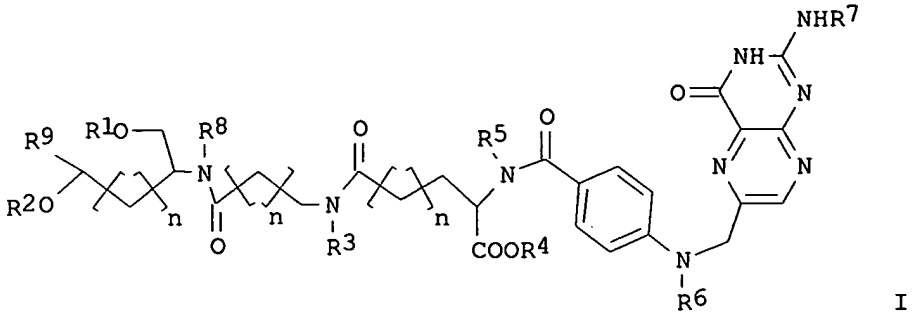
AB Provided are peptidomimetic protein-binding arrays, their manuf., use, and application. The protein-binding array elements of the invention include a peptidomimetic segment linked to a **solid** support via a stable anchor. The invention contemplates peptidomimetic array element library synthesis, distribution, and spotting of array elements onto **solid** planar substrates, labeling of complex protein mixts., and the anal. of differential protein binding to the array. The invention also enables the enrichment or purifn., and subsequent sequencing or structural anal. of proteins that are identified as differential by the array screen. Kits including proteomic microarrays in accordance with the present invention are also provided. Slides were prepd. with a reflective aluminum coating that was further overcoated with a thin **silicon** dioxide dielec., followed by APTES. The Al/**SiO2** substrate amplified the signal from Cy3/Cy5 tagged cDNA by approx. 10-40 fold relative to the corresponding glass substrate.

L23 ANSWER 5 OF 35 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2002:905731 HCAPLUS
DOCUMENT NUMBER: 138:14152
TITLE: Preparation of enzymic ribonucleic acid peptide **conjugates** as antitumor and antiviral agents and compositions for cellular delivery
INVENTOR(S): Beigelman, Leonid; Matulic-Adamic, Jasenka; Vargeese, Chandra; Karpeisky, Alexander; Blatt, Lawrence; Shaffer, Christopher
PATENT ASSIGNEE(S): Ribozyme Pharmaceuticals, Inc, USA
SOURCE: PCT Int. Appl., 220 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002094185	A2	20021128	WO 2002-US15876	20020520
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2003104985	A1	20030605	US 2002-151116	20020517
US 2003130186	A1	20030710	US 2002-201394	20020722

PRIORITY APPLN. INFO.: US 2001-292217P P 20010518
US 2001-306883P P 20010720
US 2001-311865P P 20010813
US 2002-362016P P 20020306

GI



I

AB This invention features peptide nucleotide **conjugates** I wherein each R1-R8 are independently hydrogen, alkyl, substituted alkyl, aryl, substituted aryl, or a protecting group, each "n" is independently an integer from 0 to about 200, R9 is a straight or branched chain alkyl, substituted alkyl, aryl, or substituted aryl, and R2 is a phosphorus contg. group, nucleoside, nucleotide, small mol., nucleic acid, or a **solid** support comprising a **linker**., degradable **linkers**, compns., methods of synthesis, and applications thereof, including folate, galactose, galactosamine, N-acetyl galactosamine, **PEG**, phospholipid, peptide and human serum albumin (HAS) derived **conjugates** of biol. active compds., including antibodies, antivirals, chemotherapeutics, peptides, proteins, hormones nucleosides, nucleotides, non-nucleosides, and nucleic acids including enzymic nucleic acids, DNAzymes, allozymes, antisense, dsRNA, siRNA, triplex oligonucleotides, 2,5-A chimeras, decoys and aptamers. Thus, 1-O-(4-monomethoxytrityl)-N-(12'-hydroxydodecanoyl-2-acetamido-3,4,6-tri-O-acetyl-2-deoxy-3-D-galactopyranose)-D-threoninol 3-O-(2-cyanoethyl,N,N-diisopropylphosphorami-dite) was prepd. and incorporated into RNA. A method of treating a cancer patient, comprising contacting cells of patient wherein said cancer is breast cancer, lung cancer, colorectal cancer, brain cancer, esophageal cancer, stomach cancer, bladder cancer, pancreatic cancer, cervical cancer, head and neck cancer, ovarian cancer, melanoma, lymphoma, glioma, or multidrug resistant cancers and/or viral infections including HIV, HBV, HCV, CMV, RSV, HSV, poliovirus, influenza, rhinovirus, west nile virus, Ebola virus, foot and mouth virus, and papilloma.

L23 ANSWER 6 OF 35 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2002:818292 HCAPLUS
DOCUMENT NUMBER: 138:33866
TITLE: Tethered thiazole orange intercalating dye for development of fiber-optic nucleic acid biosensors
AUTHOR(S): Wang, Xiaofeng; Krull, Ulrich J.
CORPORATE SOURCE: Chemical Sensors Group, Department of Chemistry, University of Toronto, Mississauga, ON, L5L 1C6, Can.
SOURCE: Analytica Chimica Acta (2002), 470(1), 57-70
CODEN: ACACAM; ISSN: 0003-2670
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Single-stranded DNA (ssDNA) oligonucleotide in soln., or that is immobilized onto a **surface** to create a biosensor, can be used as

a selective probe to bind to a complementary single-stranded sequence. Fluorescence enhancement of thiazole orange (TO) occurs when the dye intercalates into double-stranded DNA (dsDNA). TO dye has been covalently attached to probe oligonucleotides (homopolymer and mixed base 10mer and 20mer) through the 5' terminal phosphate group using **polyethylene glycol linker**. The tethered TO dye was able to intercalate when dsDNA formed in soln., and also at fused **silica surfaces** using immobilized ssDNA. The results indicated the potential for development of a self-contained biosensor where the fluorescent label was available as part of the immobilized oligonucleotide probe chem. The approach was shown to be able to operate in a reversible manner for multiple cycles of detection of targeted DNA sequences.

REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L23 ANSWER 7 OF 35 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2002:697526 HCAPLUS
DOCUMENT NUMBER: 137:365542
TITLE: Stabilization of penicillinase-hapten **conjugate** for enzyme immunoassay
AUTHOR(S): Omidfar, K.; Rasaee, Mohammad J.; Zaraee, Ali B.; Amir, M. Pour; Rahbarizadeh, F.
CORPORATE SOURCE: School of Medical Sciences, Department of Biochemistry, Tarbiat-Modarres University, Tehran, 14155-4838, Iran
SOURCE: Journal of Immunoassay & Immunochemistry (2002), 23(3), 385-398
CODEN: JIIOAZ; ISSN: 1532-1819
PUBLISHER: Marcel Dekker, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The influence of various additives, such as org. solvents, polyhydric alcs., salts, polymers, and cross-**linker**, on the stability and storage ability of penicillinase-morphine **conjugate** was studied in liq. and **solid** (freeze dried) states. The results of these expts. showed that using low concns. of CaCl2 (0.1-0.2%) could stabilize enzyme activity in both states for more than seven months. The immunoreactivity of antigen toward the antibody did not change significantly. However, a cross-**linker** such as glutaraldehyde and various additives such as dimethylsulfoxide, glycerol, **polyethylene glycol**, gelatin, dextran, ammonium sulfate, lactose, and sucrose did not have any effect on stability. In addn., it was found that the presence of lactose and sucrose in the lyophilization procedure gives a significant amt. of protection to the enzyme, which could last for a period of seven months and preserve almost 95% of the enzyme activity, as well as immunoreactivity of the tracer mol.

REFERENCE COUNT: 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L23 ANSWER 8 OF 35 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2002:632737 HCAPLUS
DOCUMENT NUMBER: 137:180735
TITLE: **Solid** phase sequencing of double-stranded nucleic acids by array hybridization and mass spectrometry
INVENTOR(S): Fu, Dong-Jing; Cantor, Charles R.; Koster, Hubert; Smith, Cassandra L.

PATENT ASSIGNEE(S): Boston University, USA; Sequenom, Inc.
SOURCE: U.S., 79 pp., Cont.-in-part of U.S. Ser. No. 420,009, abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 18
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6436635	B1	20020820	US 1996-614151	19960312
US 5795714	A	19980818	US 1993-110691	19930823
EP 1262564	A2	20021204	EP 2002-16384	19940106
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE				
US 5631134	A	19970520	US 1995-462704	19950605
CA 2218188	AA	19961017	CA 1996-2218188	19960410
WO 9632504	A2	19961017	WO 1996-US5136	19960410
WO 9632504	A3	19961114		
W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML				
AU 9655446	A1	19961030	AU 1996-55446	19960410
EP 830460	A1	19980325	EP 1996-912743	19960410
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI				
JP 11503611	T2	19990330	JP 1996-531243	19960410
AU 9891379	A1	19990114	AU 1998-91379	19981106
AU 738203	B2	20010913		
AU 758454	B2	20030320	AU 2000-42518	20000619
AU 761161	B2	20030529	AU 2001-91345	20011114
AU 2001091345	A5	20020103		
US 2003096258	A1	20030522	US 2002-136829	20020430

PRIORITY APPLN. INFO.:

US 1992-972012	B2	19921106
US 1993-1323	B2	19930107
US 1993-110691	A2	19930823
US 1995-419994	B2	19950411
US 1995-420009	B2	19950411
AU 1994-59929	A3	19940106
EP 1994-906047	A3	19940106
US 1994-322526	A3	19941017
US 1996-614151	A	19960312
AU 1996-55446	A3	19960410
WO 1996-US5136	W	19960410
AU 1998-51980	A3	19971106

AB This invention relates to methods for detecting and sequencing of target double-stranded nucleic acid sequences, to nucleic acid probes and arrays of probes useful in these methods, and to kits and systems which contain these probes. Useful methods involve hybridizing the nucleic acids or nucleic acids which represent complementary or homologous sequences of the target to an array of nucleic acid probes. These probe comprise a single-stranded portion, an optional double-stranded portion and a variable sequence within the single-stranded portion. The mol. wts. of the hybridized nucleic acids of the set can be detd. by mass spectroscopy,

and the sequence of the target detd. from the mol. wts. of the fragments. Nucleic acids whose sequences can be detd. include nucleic acids in biol. samples such as patient biopsies and environmental samples. Probes may be fixed to a **solid** support such as a hybridization chip to facilitate automated detn. of mol. wts. and identification of the target sequence. The invention utilizes the Sanger sequencing strategy and assembles the sequence information by anal. of the nested fragments obtained by base-specific chain termination via their different mol. masses using mass spectrometry, as for example, MALDI or ES mass spectrometry. A further increase in throughput can be obtained by introducing mass-modifications in the oligonucleotide primer, chain-terminating nucleoside triphosphates and/or in the chain-elongating nucleoside triphosphates, as well as using integrated tag sequences which allow multiplexing by hybridization of tag specific probes with mass differentiated mol. wts. The syntheses of nucleic acid primers mass modified by glycine, glycylglycine, .beta.-alanine or glycol residues at various positions on the terminal nucleosides are also provided.

REFERENCE COUNT: 57 THERE ARE 57 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L23 ANSWER 9 OF 35 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2002:332061 HCAPLUS
DOCUMENT NUMBER: 136:363880
TITLE: Synthetic regulatory compounds
INVENTOR(S): Dervan, Peter; Mapp, Anna; Ptashne, Mark; Ansari, Aseem
PATENT ASSIGNEE(S): Memorial Sloan-Kettering Cancer Center, USA; California Institute of Technology
SOURCE: PCT Int. Appl., 103 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002034295	A1	20020502	WO 2000-US29617	20001027
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 2001013481	A5	20020506	AU 2001-13481	20001027

PRIORITY APPLN. INFO.: WO 2000-US29617 A 20001027

AB This invention provides novel synthetic regulatory compds. that comprise a nucleic acid binding moiety, a linker, and a regulatory moiety, compns. comprising such compds., methods of designing and synthesizing such compds., methods of screening such compds. to identify those having the desired regulatory activity, and methods of using such compds. to prevent or treat disease in plants and animals, including humans. These compds., and compns. contg. them, have multiple applications, including use in human and animal medicine and in agriculture.

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L23 ANSWER 10 OF 35 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2002:130630 HCAPLUS
DOCUMENT NUMBER: 137:332789
TITLE: Enhanced tumor cell selectivity of adriamycin-monoclonal antibody **conjugate** via a poly(ethylene glycol)-based cleavable linker
AUTHOR(S): Suzawa, T.; Nagamura, S.; Saito, H.; Ohta, S.; Hanai, N.; Kanazawa, J.; Okabe, M.; Yamasaki, M.
CORPORATE SOURCE: Tokyo Research Laboratories, Kyowa Hakko Kogyo Co., Ltd., Machida-shi, Tokyo, 194-8533, Japan
SOURCE: Journal of Controlled Release (2002), 79(1-3), 229-242
CODEN: JCREEC; ISSN: 0168-3659
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A novel **linker** consisting of poly(ethylene glycol) (**PEG**) and dipeptide was used for **conjugation** of adriamycin with tumor-specific monoclonal antibody, NL-1, to confirm that the **linker** can be cleaved selectively with the tumor specific enzyme to express cytotoxicity of the anti-tumor agent. Initially, adriamycin-**conjugated PEG linkers** through different amino acid compns., alanyl-valine (Ala-Val), alanyl-proline (Ala-Pro), and glycyl-proline (Gly-Pro) sequences, were prepd. to confirm selective digestion with model enzymes. Adriamycin was released by particular model endoproteases, thermolysin and proline endopeptidase, from the **linkers** with different efficiency. When **conjugates** were prepd. using these adriamycin-bound **linkers, conjugates** had no loss of binding affinity and specificity for common acute lymphoblastic leukemia antigen (CALLA) expressed on the Daudi cell **surfaces** as the target of NL-1 antibody. In addn., adriamycin release from the **conjugates** was also confirmed by incubating them with specific proteases. Tumor cell growth was inhibited dose-dependently for the **conjugates** carrying Ala-Val and Gly-Pro **linkers**, whereas significant inhibitory effect was abolished for the **conjugate** carrying Ala-Pro **linker**, indicating that cytotoxic effect can be controlled by specificity of antibody and compn. of **linker** peptide. IC50 for Ala-Val linked **conjugate** was approx. 3.5 .mu.g/mL and that for Gly-Pro linked **conjugate** was 5.2 .mu.g/mL. **PEG**-dipeptidyl **linker** demonstrated here will be an effective tool for the prepn. of immunoconjugate, esp. specific activation of anti-tumor agents at desired tumor tissues.
REFERENCE COUNT: 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L23 ANSWER 11 OF 35 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2002:51665 HCAPLUS
DOCUMENT NUMBER: 136:80845
TITLE: Dipstick assays with a plurality of different probes to target double-stranded DNA in sample solution
INVENTOR(S): Lee, Helen; Dineva, Magda Anastassova
PATENT ASSIGNEE(S): UK
SOURCE: PCT Int. Appl., 57 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent

LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002004667	A2	20020117	WO 2001-GB3021	20010706
WO 2002004667	A3	20021227		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

EP 1301627	A2	20030416	EP 2001-945536	20010706

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR

PRIORITY APPLN. INFO.: GB 2000-16813 A 20000707
WO 2001-GB3021 W 20010706

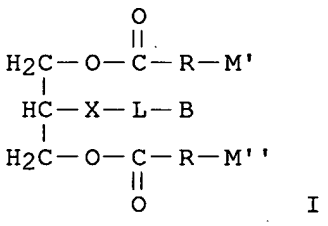
AB Improved dipstick assays for testing for the presence of a target nucleic acid in a sample soln. are described. A dipstick is provided which comprises a contact end for contacting the sample soln. and a capture zone remote from the contact end for capturing target nucleic acid. Sample soln. is contacted with the contact end to cause sample soln. to move by capillary action to the capture zone. Target nucleic acid in the sample soln. is captured at the capture zone and is detected by a plurality of different labeled detection probes each capable of hybridizing to a different region of the target nucleic acid. The detection signal is thereby enhanced. In other methods a plurality of different capture probes are added to the sample soln. which can then be bound by a capture moiety at the capture zone to indirectly capture target nucleic acid. A detection probe capable of hybridizing to the target nucleic acid which can be releasably immobilized to a probe zone between the contact end and capture zone of the the dipstick is another embodiment of the invention. Also, the nucleic acid of interest could be coupled to a plurality of labels or ligands which can be bound by a ligand binding moiety to detect or capture the target nucleic acid when the probe has hybridized to the target nucleic acid. Furthermore, a linker could covently couple the label or ligand to the nucleic acid with a spacer. Capture of target nucleic acid is thereby improved. Using this method about 104 copies of Chyamydia trachomatis elementary bodies could be detected in less than an hour including the sample prepn. step. Although this assay has a sensitivity of detected about equal to other sandwich hybridization assays, it has the major advantages of speed and simplicity. Kits and dipsticks for carrying out such methods are also described.

L23 ANSWER 12 OF 35 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2001:731185 HCAPLUS
DOCUMENT NUMBER: 135:269295
TITLE: Labeled, immobilizable triacylglycerol analogs for lipase assays
INVENTOR(S): Price-Jones, Molly Jean; James, David Martin; Fowler, Anne; Poulsen, Fritz; Tornquist, Hans; Hawes, Calvin Richard

PATENT ASSIGNEE(S): Amersham Pharmacia Biotech UK Limited, UK
SOURCE: PCT Int. Appl., 28 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001073442	A1	20011004	WO 2001-GB1350	20010323
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1269192	A1	20030102	EP 2001-915508	20010323
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				

PRIORITY APPLN. INFO.: GB 2000-7465 A 20000329
WO 2001-GB1350 W 20010323
OTHER SOURCE(S): MARPAT 135:269295
GI



I

AB Disclosed is a triacylglycerol analog (I; L = **linker**; B = binding agent; X = atom or group suitable for attaching L to the glycerol chain; R = C8-30-straight chain satd. or unsatd. alkyl group substituted with M' or M" wherein at least one of M' and/or M" is a detectable label). The compd. can be used as a lipase substrate in a **solid** phase-based assay system, such as a scintillation proximity assay, to detect lipase enzyme activity. Thus, I (L = **PEG**, B = biotin, X = NH, R = tritium-labeled heptadecyl, M,M' = tritium) was synthesized, immobilized on streptavidin-coated YSi beads, and used in scintillation proximity assays of various lipases.
REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L23 ANSWER 13 OF 35 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2001:625600 HCAPLUS
DOCUMENT NUMBER: 136:406733
TITLE: Protein delivery from materials formed by

self-selective **conjugate** addition reactions
AUTHOR(S): Elbert, D. L.; Pratt, A. B.; Lutolf, M. P.; Halstenberg, S.; Hubbell, J. A.
CORPORATE SOURCE: Swiss Federal Institute of Technology and University of Zurich, Institute for Biomedical Engineering and Department of Materials, Zurich, CH-8044, Switz.
SOURCE: Journal of Controlled Release (2001), 76(1-2), 11-25
CODEN: JCREEC; ISSN: 0168-3659
PUBLISHER: Elsevier Science Ireland Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A new chem. crosslinking scheme was utilized for the formation of degradable poly(ethylene glycol) hydrogels suitable for the delivery of protein drugs. An aq. soln. contg. a **PEG**-multiacrylate and **solid** particles of albumin was mixed with an aq. soln. contg. a **PEG**-dithiol, rapidly producing a cross-linked hydrogel through a Michael-type addn. reaction. For some formulations, it was obsd. that about 65% of the incorporated protein was released with zero-order kinetics over a period of about 4 days. By changing the functionality of the cross-**linker**, the release of protein could even be delayed for about 4 days, followed by zero-order release. The mechanism for release appeared to be a combination of slow dissoln. of protein in the presence of **PEG** and hindered diffusion of protein through the gel. The crosslinking of the gels was studied rheometrically, and the hydrolytic degrdn. of the gels was characterized by measuring the swelling of the gels. Biochem. anal. of the released proteins demonstrated that the polymers reacted with each other, but not with proteins. Utilizing the Flory-Rehner and Peppas-Merrill equations, a framework for modeling the protein release from the gels is described.
REFERENCE COUNT: 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L23 ANSWER 14 OF 35 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2001:572407 HCAPLUS
DOCUMENT NUMBER: 136:284320
TITLE: Tumor targeting using anti-HER2 immunoliposomes
AUTHOR(S): Park, J. W.; Kirpotin, D. B.; Hong, K.; Shalaby, R.; Shao, Y.; Nielsen, U. B.; Marks, J. D.; Papahadjopoulos, D.; Benz, C. C.
CORPORATE SOURCE: Division of Hematology/Oncology, Department of Medicine, University of California (UCSF), San Francisco, CA, 94143-0324, USA
SOURCE: Journal of Controlled Release (2001), 74(1-3), 95-113
CODEN: JCREEC; ISSN: 0168-3659
PUBLISHER: Elsevier Science Ireland Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB We have generated anti-HER2 (ErbB2) immunoliposomes (ILs), consisting of long circulation liposomes linked to anti-HER2 monoclonal antibody (MAb) fragments, to provide targeted drug delivery to HER2-overexpressing cells. Immunoliposomes were constructed using a modular strategy in which components were optimized for internalization and intracellular drug delivery. Parameters included choice of antibody construct, antibody d., antibody **conjugation** procedure, and choice of liposome construct. Anti-HER2 immunoliposomes bound efficiently to and internalized in HER2-overexpressing cells in vitro as detd. by fluorescence microscopy, electron microscopy, and quant. anal. of

fluorescent probe delivery. Delivery via ILs in HER2-overexpressing cells yielded drug uptake that was up to 700-fold greater than with non-targeted sterically stabilized liposomes. In vivo, anti-HER2 ILs showed extremely long circulation as stable constructs in normal adult rats after a single i.v.dose, with pharmacokinetics that were indistinguishable from sterically stabilized liposomes. Repeat administrations revealed no increase in clearance, further confirming the ILs retain the long circulation and non-immunogenicity of sterically stabilized liposomes. In five different HER2-overexpressing xenograft models, anti HER2 ILs loaded with doxorubicin (dox) showed potent anticancer activity, including tumor inhibition, regressions, and cures (pathol. complete responses). ILs were significantly superior vs. all other treatment conditions tested: free dox, liposomal dox, free MAb (trastuzumab), and combinations of doc+MAb or liposomal dox+MAb. For example, ILs produced significantly superior antitumor effects vs. non-targeted liposomes (P value from <0.0001 to 0.04 in eight sep. expts.). In a non-HER2-overexpressing xenograft model (MCF7), ILs and non-targeted liposomal dox producted equiv. antitumor effects. Detailed studies of tumor localization indicated a novel mechanism of drug delivery for anti-HER2 ILs. Immunotargeting did not increase tumor tissue levels of ILs vs. liposomes, as both achieved very high tumor localization (7.0-8.5% of injected dose/ g tissue) in xenograft tumors. However, histol. studies using colloidal-**gold** labeled ILs demonstrated efficient intracellular delivery in tumor cells, while non-targeted liposomes accumulated within stroma, either extracellularly or within macrophages. In the MCF7 xenograft model lacking HER2-overexpression, no difference in tumor cell uptake was seen, with both ILs and non-targeted liposomes accumulating within stroma. Thus, anti-HER2 ILs, but not non-targeted liposomes, achieve intracellular drug delivery via receptor mediated endocytosis, and this mechanism is assocd. with superior antitumor activity. Based on these results, anti-HER2 immunoliposomes have been developed toward clin. trials. Reengineering of construct design for clin. use has been achieved, including: new anti-HER2 scFv F5 generated by screening of a phage antibody library for internalizing anti-HER2 phage antibodies; modifications of the scFv expression construct to support large scale prodn. and clin. use and development of methods for large-scale **conjugation** of antibody fragments with liposomes. We developed a scalable two-step protocol for linkage of scFv to performed and drug-loaded liposomes. Our final, optimized anti-HER2 ILs-dox construct consists of F5 **conjugated** to derivatized **PEG**-PE **linker** and incorporated into com. available liposomal doxorubicin (Doxil). Finally, further studies of the mechanism of action of anti-HER2 ILs-dox suggest that this strategy may provide optimal delivery of anthracycline-based chemotherapy to HER2-overexpressing cancer cells in the clinic, while circumventing the cardiotoxicity assocd. with trastuzumab + anthracycline. We conclude that anti-HER2 immunoliposomes represent a promising technol. for tumor-targeted drug delivery, and that this strategy may also applicable to other receptor targets and/or using other delivered agents.

REFERENCE COUNT: 52 THERE ARE 52 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L23 ANSWER 15 OF 35 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2001:453593 HCAPLUS
DOCUMENT NUMBER: 135:185325
TITLE: Different Strategies for Formation of PEGylated EGF-**Conjugated** PEI/DNA Complexes for Targeted Gene Delivery

AUTHOR(S): Blessing, Thomas; Kursa, Malgorzata; Holzhauser, Robert; Kircheis, Ralf; Wagner, Ernst
CORPORATE SOURCE: Institute of Medical Biochemistry, University of Vienna, Vienna, A-1030, Austria
SOURCE: Bioconjugate Chemistry (2001), 12(4), 529-537
CODEN: BCCHES; ISSN: 1043-1802
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English

AB With the aim of generating gene delivery systems for tumor targeting, we synthesized a **conjugate** consisting of polyethyleneimine (PEI) covalently modified with epidermal growth factor (EGF) peptides. Transfection efficiency of the **conjugate** was evaluated and compared to native PEI in 3 tumor cell lines: KB epidermoid carcinoma cells, CMT-93 rectum carcinoma cells, and Renca-EGFR renal carcinoma cells. Depending on the tumor cell line, incorporation of EGF resulted in an up to 300-fold increased transfection efficiency. This ligand-mediated enhancement and competition with free EGF strongly suggested uptake of the complexes through the EGF receptor-mediated endocytosis pathway. Shielded particles being crucial for systemic gene delivery, we studied the effect of covalent **surface** modification of EGF-PEI/DNA complexes with a **PEG** deriv. An alternative way for the formation of PEGylated EGF-contg. complexes was also evaluated where EGF was projected away from PEI/DNA core complexes through a **PEG linker**. Both strategies led to shielded particles still able to efficiently transfect tumor cells in a receptor-dependent fashion. These PEGylated EGF-contg. complexes were 10- to 100-fold more efficient than PEGylated complexes without EGF.

REFERENCE COUNT: 61 THERE ARE 61 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L23 ANSWER 16 OF 35 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2001:380754 HCAPLUS
DOCUMENT NUMBER: 134:371853
TITLE: Blood-compatible polymer **surfaces** for usage in medical devices
INVENTOR(S): Nowak, Goetz; Bucha, Elke
PATENT ASSIGNEE(S): Haemosys G.m.b.H., Germany
SOURCE: PCT Int. Appl., 24 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001036613	A1	20010525	WO 2000-EP11253	20001114
W: CA, JP, US				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR				
DE 19955341	A1	20010802	DE 1999-19955341	19991117
EP 1282695	A1	20030212	EP 2000-989856	20001114
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY, TR				
JP 2003515110	T2	20030422	JP 2001-538492	20001114

PRIORITY APPLN. INFO.: DE 1999-19955341 A 19991117

WO 2000-EP11253 W 20001114

AB The invention relates to a blood-compatible **surface** comprising a polymer **surface** and a plurality of **conjugates** made of **linkers** and active agents immobilized thereon. The polymer **surface** contains similar or different structural units that carry carbonyl groups. The **linkers** contain a structural element that is able to form a hydrogen bridge bond. A polyorganosiloxane acting as the active agent is linked to the **linkers**. Thus polymethylmethacrylate particles were coated with dimethylpolysiloxane-**PEG**; R-hirudin contg. blood was contacted with the particles; no loss of blood platelets was obsd., while in the control expt. (particles without dimethylpolysiloxane coating) substantial platelet no. fluctuation was obsd.

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L23 ANSWER 17 OF 35 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2001:183381 HCAPLUS
DOCUMENT NUMBER: 134:367843
TITLE: An enzyme-labile safety catch linker for synthesis on a soluble polymeric support
AUTHOR(S): Grether, Uwe; Waldmann, Herbert
CORPORATE SOURCE: Max-Planck-Institute fur molekulare Physiologie Abteilung Chemische Biologie, Dortmund, 44227, Germany
SOURCE: Chemistry--A European Journal (2001), 7(5), 959-971
CODEN: CEUJED; ISSN: 0947-6539
PUBLISHER: Wiley-VCH Verlag GmbH
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The development of new and broadly applicable linker groups which are stable under a variety of reaction conditions and allow release of the desired products from the **solid** support under very mild conditions is of great interest in org. synthesis and combinatorial chem. We describe an enzyme-labile safety-catch linker which releases alcs. and amines through (i) enzymic cleavage of an amino group and (ii) subsequent lactam formation. The linker group was investigated on different polymeric supports: TentaGel, PEGA, CPG-beads and the sol. polymer POE-6000. From these linker-polymer **conjugates** 2-methoxy-5-nitrobenzyl alc. was released by penicillin G acylase catalyzed cleavage of a phenylacetamide and attack of the liberated benzylamine on the neighboring ester group in ortho position. The model study revealed that only in the case of sol. POE-6000 **conjugate** high yields for the cleavage could be achieved. In the case of the other **solid** supports the enzyme does not have access to the interior of the polymer matrix. The application of the POE-6000 linker **conjugate** was investigated for various esters in Pd0-catalyzed Heck-, Suzuki- and Sonogashira reactions as well as in a Mitsunobu reaction and cycloaddns. These studies proved that the linker is stable under a broad variety of reaction conditions and that the enzymic method allows for release of the desired product alcs. under extremely mild conditions at pH 7 and 37.degree.C. In addn., the enzymic reaction proceeds with complete chemoselectivity, that is other esters or amides are not attacked by the biocatalyst. In addn. to alcs. amines can also be cleaved by means of the enzyme-initiated two-step process. In these cases the higher stability of amides as compared to esters requires warming to 60.degree.C to induce cyclization and release of the desired product.

REFERENCE COUNT: 55 THERE ARE 55 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L23 ANSWER 18 OF 35 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2001:115683 HCAPLUS
DOCUMENT NUMBER: 134:315979
TITLE: Steric Stabilization of Fusogenic Liposomes by a Low-pH Sensitive PEG-Diortho Ester-Lipid **Conjugate**
AUTHOR(S): Guo, X.; Szoka, F. C., Jr.
CORPORATE SOURCE: Departments of Pharmaceutical Chemistry and Biopharmaceutical Sciences, University of California at San Francisco, San Francisco, CA, 94143-0446, USA
SOURCE: Bioconjugate Chemistry (2001), 12(2), 291-300
CODEN: BCCHES; ISSN: 1043-1802
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
AB We describe the synthesis and characterization of a pH-sensitive poly(ethylene glycol)-diortho ester-distearoyl glycerol **conjugate** (POD). POD was prepd. by a one-step synthesis, and its acid sensitivity characterized by TLC. The **conjugate** was found to be stable at neutral pH for greater than 3 h but degraded completely within 1 h at pH 5. Liposomes composed of 10% of POD and 90% of a fusogenic lipid, dioleoyl phosphatidylethanolamine (DOPE) were readily prepd. and remained stable for up to 12 h in neutral buffer as shown by photon correlation spectrometry and a liposome contents leakage assay. However, when POD/DOPE liposomes were incubated in acidic pH as mild as 5.5, they aggregated and released most of their contents within 30 min. The kinetics of content release from POD/DOPE liposomes consisted of two phases, a lag phase, and a burst phase. The lag phase is inversely correlated with pH and the logarithm of the length of lag phase showed a linear relationship with the buffer pH. When the POD/DOPE liposomes were incubated in 75% of fetal bovine serum at 37 .degree.C, they remained as stable as traditional **PEG**-grafted liposomes for 12 h but released 84% of the encapsulated ANTS in the following 4 h. Upon i.v. administration into mice, liposomes composed of 10% POD and 90% DOPE were cleared from circulation by a one-compartment kinetics with a half-life of about 200 min. POD is an example for the design of a novel category of pH sensitive lipids composed of a headgroup, an acid-labile diortho ester **linker** and a hydrophobic tail. The uniquely fast degrdn. kinetics of POD at pH 5-6 and its ability to stabilize liposomes in serum make the **conjugate** suitable for applications for triggered drug release systems targeted to mildly acidic bio-environments such as endosomes, **solid** tumors, and inflammatory tissues.
REFERENCE COUNT: 44 THERE ARE 44 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L23 ANSWER 19 OF 35 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2000:645678 HCAPLUS
DOCUMENT NUMBER: 133:190191
TITLE: Process of desorption of linker-bound substances from a polymeric **surface** using a polar organic solvent
INVENTOR(S): Gotz, Nowak; Bucha, Elke
PATENT ASSIGNEE(S): Haemosys G.m.b.H., Germany
SOURCE: Eur. Pat. Appl., 9 pp.
CODEN: EPXXDW

DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

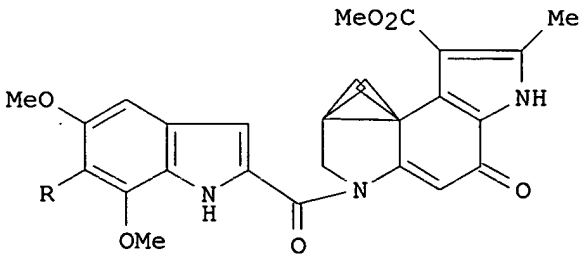
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1035130	A1	20000913	EP 2000-104418	20000303
EP 1035130	B1	20021009		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
DE 19909584	A1	20000914	DE 1999-19909584	19990304
AT 225802	E	20021015	AT 2000-104418	20000303
JP 2000297166	A2	20001024	JP 2000-59898	20000306

PRIORITY APPLN. INFO.: DE 1999-19909584 A 19990304

AB The invention concerns the desorption of **linker**-bound biol. substances from a polymeric adsorbent using polar org. solvents, e.g. alkanols and esters at up to 60 vol./vol.%. Thus hirudin-**PEG** bound to polymethylmethacrylate was eluted with a 40 vol./vol.% methanol soln.; the adsorbent could be reused for a further binding process.

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L23 ANSWER 20 OF 35 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2000:564511 HCAPLUS
DOCUMENT NUMBER: 133:335107
TITLE: Synthesis of a novel duocarmycin derivative DU-257 and its application to immunoconjugate using poly(ethylene glycol)-dipeptidyl linker capable of tumor specific activation
AUTHOR(S): Suzawa, T.; Nagamura, S.; Saito, H.; Ohta, S.; Hanai, N.; Yamasaki, M.
CORPORATE SOURCE: Tokyo Research Laboratories, Kyowa Hakko Kogyo Co., Ltd, Tokyo, 194-8533, Japan
SOURCE: Bioorganic & Medicinal Chemistry (2000), 8(8), 2175-2184
CODEN: BMECEP; ISSN: 0968-0896
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



I

AB Novel anti-tumor agent, duocarmycin deriv. DU-257 [I; R = H2NCH2CH2O, (II)], was designed and synthesized to prep. immunoconjugate in order to confirm the feasibility of enzymically cleavable **linker** consisting of poly(ethylene glycol) (**PEG**) and dipeptide, L-alanyl-L-valine. Oxyethylamine arm was introduced at 4-methoxy position of segment B of DU-86 [I; R = OMe, (III)] to form II and evaluated its property. II retained similar stability and potency with III while enhanced hydrophilicity suggested. II was condensed to the **PEG** -dipeptidyl **linker** through carboxyl terminal of dipeptide, and enzymic release of II using a model enzyme, thermolysin, similar enzyme of which was shown to be overexpressed at various tumor sites, was evaluated by HPLC anal. Cleavage between the **linker** amino acids by the model protease and release of II as valine **conjugated** form was confirmed. The enzymically released form of II expressed its cytotoxicity without loss of the potency for HeLaS3 and SW1116 tumor cell lines, although the efficacy was different in individual cells. II was then **conjugated** through the **linker** to KM231 monoclonal antibody specifically reactive to GD3 antigen which was shown to be expressed on the **surface** of many malignant tumors such as SW1116. The **conjugate** retained its binding specificity for SW1116 cell with a similar activity with KM231. Furthermore, the **conjugate** showed significant growth inhibition on SW1116 cell at a concn. of 75 .mu.g/mL while no effect on antigen neg. cell, HeLaS3. These results suggest that the **conjugate** retained its anti-tumor effect only when it bound on and was activated at the target cell, simultaneously. II will be one of the candidate of anti-tumor agent for application to immunoconjugate and its **conjugate** with KM231 via **PEG**-dipeptidyl **linker** will be a useful entity for cancer therapy related to sLea expression.

REFERENCE COUNT: 40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L23 ANSWER 21 OF 35 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1999:708644 HCAPLUS
DOCUMENT NUMBER: 131:327539
TITLE: PEG-LHRH analog **conjugates**
INVENTOR(S): El Tayar, Nabil; Zhao, Xuan; Bentley, Michael D.
PATENT ASSIGNEE(S): Applied Research Systems ARS Holding N. V., Neth. Antilles
SOURCE: PCT Int. Appl., 21 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9955376	A1	19991104	WO 1999-US9160	19990428
W: AU, CA, IL, JP, US				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
CA 2330448	AA	19991104	CA 1999-2330448	19990428
AU 9938696	A1	19991116	AU 1999-38696	19990428
AU 760381	B2	20030515		
EP 1075282	A1	20010214	EP 1999-921497	19990428
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,				

IE, FI

JP 2002512982	T2	20020508	JP 2000-545573		19990428
US 6433135	B1	20020813	US 2000-698134		20001030
US 2002183257	A1	20021205	US 2002-184126		20020628
PRIORITY APPLN. INFO.:			US 1998-83340P	P	19980428
			WO 1999-US9160	W	19990428
			US 2001-968134	A3	20010929

AB **PEG**-LHRH analog **conjugates** are provided in which a **PEG** moiety is covalently bound to the OH of a serine residue of an LHRH analog either directly or via a bifunctional **linker** mol. such as an amino acid. The **conjugate** is subject to hydrolysis at physiol. pH or by esterases in the blood, thereby releasing free LHRH analog, which acts physiol. as an LH agonist or antagonist. The **conjugates** show good soly. in aq. media. The **conjugates** are prepd. by reaction of an LHRH analog with a PEGylating agent such as Me(OCH2CH2)mO(CH2)nCO2Z (n = 1-3; Z = N-succinimidyl or other activating group), or by total **solid**-phase synthesis using a PEGylated serine in place of serine. Thus, a Me-**PEG**-antide **conjugate** with the **PEG** chain bound to Ser4 dissolved in water to the extent of >30 mg/mL and was hydrolyzed at 37.degree. and pH 7.2 with a half-life of 5.56 h.

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L23 ANSWER 22 OF 35 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1999:234084 HCAPLUS
DOCUMENT NUMBER: 130:264437
TITLE: Preparing **conjugates** using **polyethylene glycol linkers**
INVENTOR(S): Davis, Kenneth A.; Bishop, James E.
PATENT ASSIGNEE(S): Becton, Dickinson and Company, USA
SOURCE: PCT Int. Appl., 13 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9917120	A1	19990408	WO 1998-US19716	19980921
W: AU, CA, JP				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
AU 9894021	A1	19990423	AU 1998-94021	19980921
PRIORITY APPLN. INFO.:			US 1997-938986	19970926
			WO 1998-US19716	19980921

AB The instant invention presents a rapid, simple method for prepg. **solid** phases, preferably beads, with antigens or other substituents presented on the **surface** in such a manner that the antigens/substituents retain their original functionality and conformation, as well as much of their native structure, to permit their use in a wide array of applications. Specifically, the substituent is attached to the **surface** of the **solid** phase by using a bifunctional deriv. of polyethylene glycol. The polyethylene glycol (PEG) acts not only to facilitate the attachment of the substituent to the **solid surface**, but also acts as a buffer to prevent or

reduce any interaction of the **solid surface** with the attached substituent or, indeed, with any other biol. compds. to which it may become exposed during the use of the **solid surface conjugates**. Phycoerythrin was **conjugated** to polymethacrylate amino beads using OPSS-PEG-SPA.
REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L23 ANSWER 23 OF 35 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1999:7808 HCAPLUS
DOCUMENT NUMBER: 130:71528
TITLE: Adenovirus Knob-domain coated nanospheres for intracellular drug and gene delivery
INVENTOR(S): Mao, Hai-quan; Wang, Yan; Byrne, Barry; Leong, Kam W.
PATENT ASSIGNEE(S): The Johns Hopkins University, USA
SOURCE: PCT Int. Appl., 21 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9856363	A1	19981217	WO 1998-US12126	19980611
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9878365	A1	19981230	AU 1998-78365	19980611
EP 988030	A1	20000329	EP 1998-926552	19980611
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				

PRIORITY APPLN. INFO.: US 1997-49496P P 19970613
WO 1998-US12126 W 19980611

AB The isolation and purifn. of adenovirus fiber protein Knob domain is taught, as well as its use as a ligand for intracellular delivery of bioactive agents, such as low mol. drugs, proteins, antisense oligonucleotides, and plasmid DNAs. The **conjugation** of Knob to the **surface** of DNA-nanospheres facilitates the binding of nanospheres to cell **surfaces** and enhances transfection efficiency of DNA-nanospheres.
REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L23 ANSWER 24 OF 35 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1998:627617 HCAPLUS
DOCUMENT NUMBER: 130:7374
TITLE: Camptothecin delivery systems. Enhanced efficacy and tumor accumulation of camptothecin following its **conjugation** to **polyethylene glycol** via a glycine **linker**
AUTHOR(S): Conover, Charles D.; Greenwald, Richard B.; Pendri,

Annapurna; Gilbert, Karl W.; Shum, Kwok L.
CORPORATE SOURCE: Research Development, Enzon Inc., Piscataway, NJ, 08854, USA
SOURCE: Cancer Chemotherapy and Pharmacology (1998), 42(5), 407-414
CODEN: CCPHDZ; ISSN: 0344-5704
PUBLISHER: Springer-Verlag
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The circulatory retention, antitumor activity, and tissue biodistribution of polyethylene glycol(PEG)-**conjugated** camptothecin-20-O-glycinate, PEG-.beta.-camptothecin (PEG-.beta.-CAPT), was assessed. Circulatory retention studies were performed in mice injected i.v. with 875 mg/kg of PEG-.beta.-CAPT. Antitumor activity was evaluated both i.p. and i.v. in mouse xenograft models. Biodistribution studies were performed in mice bearing colorectal carcinoma xenografts with 3H-labeled PEG-.beta.-CAPT and CAPT injected i.v. PEG-.beta.-CAPT had a blood t1/2.alpha. of 6 min and a t1/2.beta. of 10.2 h. Antitumor activity was seen in all treated xenograft models. PEG-.beta.-CAPT in saline provided more available labeled CAPT in the circulation than unconjugated CAPT dissolved in intralipid. More labeled CAPT accumulated in **solid** tumors when delivered in the PEG-.beta.-CAPT form, with greater preference for tumor tissue than normal tissue.

REFERENCE COUNT: 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L23 ANSWER 25 OF 35 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1998:163620 HCAPLUS
DOCUMENT NUMBER: 128:229362
TITLE: Novel combination preparations and their use in immunodiagnosis and immunotherapy
INVENTOR(S): Bohlen, Heribert
PATENT ASSIGNEE(S): Viva Diagnostika Diagnostische Produkte G.m.b.H., Germany; Bohlen, Heribert
SOURCE: PCT Int. Appl., 125 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9808875	A1	19980305	WO 1997-EP4493	19970818
W: AU, BR, BY, CA, CN, CZ, HU, IL, JP, KR, MX, NO, NZ, PL, RU, SI, SK, UA, US				
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
DE 19634730	A1	19980305	DE 1996-19634730	19960828
DE 19703699	A1	19980806	DE 1997-19703699	19970203
AU 9741193	A1	19980319	AU 1997-41193	19970818

PRIORITY APPLN. INFO.: DE 1996-19634730 19960828
DE 1997-19703699 19970203
WO 1997-EP4493 19970818

AB Combination prepns. comprising 3 components are provided for specific purposes in immunol., diagnosis, and therapy. The combination is based on the universal use of an immunolinker which can link .gtoreq.2 other different components provided with different determinants. The

immunolinker may be an inert particle bearing reagents specific for .gtoreq.2 determinants, a bispecific antibody, a protein, etc. One of the other components is a target-specific immunol. reagent bearing an antigenic determinant, e.g. a hapten, epitope, paratope, or idiotope specific for 1 of the **linker** reagents as well as a target-specific reagent (protein, Ig, antibody, antibody fragment, ligand, lectin, receptor-binding mol., adhesion mol., cytokine, etc.). The 3rd component is a biol. active or detectable substance (enzyme, radiolabel, contrast agent, cytostatic agent, prodrug, adhesion mol., cytokine, ligand, antibody, etc.) bearing a determinant specific for the other reagent on the **linker**. Thus, mice were immunized with both 2,4-dinitrophenol (DNP) and digoxigenin, and myeloma cells and spleen cells from the immunized mice were fused by the **PEG** method to provide hybridoma cells which were selected for prodn. of monoclonal antibodies to DNP or digoxigenin. Cells from the 2 hybridoma lines were then fused and selected for prodn. of bispecific antibodies to DNP and digoxigenin. The bispecific antibody was used in combination with a DNP-labeled OKT (anti-CD3) monoclonal antibody and a digoxigenin-labeled anti-CD19 monoclonal antibody for incubation with cytotoxic T-cells and Eu-labeled Epstein-Barr virus-immortalized B-cells in a cytotoxic FIA.

REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L23 ANSWER 26 OF 35 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1997:576643 HCAPLUS
DOCUMENT NUMBER: 127:185845
TITLE: Non-immunogenic cellular compositions comprised of cells with attached non-immunogenic compounds, and uses thereof
INVENTOR(S): Byun, Si-Myung; Eaton, John; Jeong, Seong-Tae; Scott, Mark D.
PATENT ASSIGNEE(S): Biomedical Frontiers, Inc., USA; Seaborn, George Stephen; Byun, Si-Myung; Eaton, John; Jeong, Seong-Tae; Scott, Mark D.
SOURCE: PCT Int. Appl., 63 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9728254	A1	19970807	WO 1997-IB139	19970203
W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
US 5908624	A	19990601	US 1996-671452	19960627
AU 9715552	A1	19970822	AU 1997-15552	19970203
EP 901521	A1	19990317	EP 1997-901754	19970203
R: CH, DE, ES, FR, GB, IT, LI, NL				
JP 2000505423	T2	20000509	JP 1997-527447	19970203

PRIORITY APPLN. INFO.: KR 1996-2440 19960201
US 1996-671452 19960627
WO 1997-IB139 19970203

AB The present invention is directed to a non-immunogenic cellular compn. comprising: a cell having a cell **surface** and antigenic determinants on the cell **surface**; an optional **linker** mol. covalently attached to the cell **surface**; and a non-immunogenic compd. (e.g. **polyethylene glycol** or a deriv. thereof) covalently attached to the **linker** mol. or directly to the cell. In one embodiment, the **linker** mol. is covalently attached directly to the antigenic determinant on the cell **surface**. In an alternative embodiment, the **linker** mol. may be covalently attached to a non-antigenic site on the cell **surface**. Various uses of the resulting non-immunogenic cell are also provided, including a method of decreasing phagocytosis of a cell, a method of decreasing an adverse reaction to a transfusion, a method of decreasing rejection of a transplanted cell, tissue or organ, and a method of decreasing antibody-induced aggregation of cells.

L23 ANSWER 27 OF 35 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1997:224428 HCAPLUS
DOCUMENT NUMBER: 126:268452
TITLE: Preparation and characterization of oligosaccharide- and oligopeptide-bearing Stealth liposomes
AUTHOR(S): Gittelman, Joshua; Harding, Jennifer; Mullah, Nasreen; Guo, Luke; DeFrees, Shawn; Zalipsky, Samuel
CORPORATE SOURCE: SEQUUS Pharmaceuticals, Inc., Menlo Park, CA, 94025, USA
SOURCE: Polymer Preprints (American Chemical Society, Division of Polymer Chemistry) (1997), 38(1), 607
CODEN: ACPPAY; ISSN: 0032-3934
PUBLISHER: American Chemical Society, Division of Polymer Chemistry
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Thiol-**PEG**-distearoylphosphatidylethanolamine was coupled with bromoacetylated peptide YIGSR or with sialyl-Lex oligosaccharide to provide a cell-adhesive ligand coupled via a **PEG linker** to a lipid anchor. These **conjugates** were combined with phosphatidylcholine, cholesterol, and methoxy-**PEG** -phosphatidylethanolamine to form unilamellar vesicles. These vesicles had 55% of the YIGSR, or 63% of the sialyl-Lex, ligands on the outer **surface**. Incubation of the YIGSR or sialyl-Lex **conjugates** with preformed liposomes resulted in localization of all the ligand on the outer **surface**.

L23 ANSWER 28 OF 35 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1995:751215 HCAPLUS
DOCUMENT NUMBER: 123:208673
TITLE: Preparation of long-circulating immunoliposomes containing adriamycin by a novel method to coat immunoliposomes with poly(ethylene glycol)
AUTHOR(S): Suzuki, Shinya; Watanabe, Satoko; Masuko, Takashi; Hashimoto, Yoshiyuki
CORPORATE SOURCE: Department of Hygienic Chemistry, Faculty of pharmaceutical Sciences, Tohoku University, Aobayama, Sendai, 980-77, Japan

SOURCE: Biochimica et Biophysica Acta (1995), 1245(1), 9-16
CODEN: BBACAQ; ISSN: 0006-3002
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Modifications of liposomes with poly (ethylene glycol) (**PEG**) have been reported to prolong blood circulation time of liposomes. In this report, an adriamycin-encapsulated immunoliposomes were modified with **PEG** by two different approaches: one is the pre-coating method using lipid deriv. of **PEG** as described by Allen et al. The other is post-coating method which is presented here. The former pre-coating method did not allow coupling of antibody due to the steric hindrance of **PEG** which had been introduced on liposome **surface**. On the other hand, in the later post-coating method, **PEG**-succinylcysteine was synthesized and was successfully **conjugated** with immunoliposomes via maleimido **linker**. Resultant **PEG**-coated immunoliposomes contg. adriamycin retained their binding activity and cytotoxicity to target cells, and also showed significantly prolonged blood circulating time as compared with conventional immunoliposomes. This is a novel method to coat immunoliposomes with **PEG**.

L23 ANSWER 29 OF 35 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1995:675079 HCAPLUS
DOCUMENT NUMBER: 124:9452
TITLE: Very large scale immobilized polymer synthesis using combinatorial arrays
INVENTOR(S): Fodor, Stephen P. A.; Stryer, Lubert; Pirrung, Michael C.; Read, J. Leighton
PATENT ASSIGNEE(S): Affymax Technologies N.V., Neth. Antilles
SOURCE: U.S., 91 pp. Cont.-in-part of U.S. 5,143,854.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 20
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5424186	A	19950613	US 1991-805727	19911206
US 5143854	A	19920901	US 1990-492462	19900307
EP 1046421	A2	20001025	EP 2000-202667	19911120
EP 1046421	A3	20010919		
EP 1046421	B1	20030702		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE				
US 5527681	A	19960618	US 1992-972007	19921105
US 6420169	B1	20020716	US 1994-348471	19941130
US 6506558	B1	20030114	US 1995-563759	19951129
US 5770456	A	19980623	US 1996-647618	19960513
US 6379895	B1	20020430	US 2000-654435	20000901
US 6416952	B1	20020709	US 2000-654206	20000901
US 6403320	B1	20020611	US 2000-684377	20001005
US 2002137096	A1	20020926	US 2001-14716	20011214
US 2003008302	A1	20030109	US 2002-77070	20020214
US 2003108899	A1	20030612	US 2002-190951	20020708

PRIORITY APPLN. INFO.: US 1989-362901 B2 19890607
US 1990-492462 A2 19900307

US 1990-624120	A2	19901206
US 1989-435316	A	19891113
US 1990-612671	A	19901113
US 1990-624114	B1	19901206
US 1990-626730	A	19901206
EP 1992-903279	A3	19911120
US 1991-796243	A	19911122
US 1991-796727	A2	19911122
US 1991-805727	A2	19911206
US 1992-972007	A1	19921105
US 1993-168904	B3	19931215
US 1994-348471	A1	19941130
US 1996-670118	A1	19960625
US 1997-829893	A1	19970402
US 1998-56927	A1	19980408
US 2000-557875	A1	20000424
US 2001-14716	A1	20011214

OTHER SOURCE(S): CASREACT 124:9452

AB A method is claimed for synthesizing oligonucleotides on a **solid** phase comprising the steps of: (a) providing a substrate as the **solid** phase, wherein said substrate comprises oligonucleotide mols. immobilized on a **surface** thereof, said oligonucleotide mols. coupled to a photoremovable protecting group; (b) irradiating a first predefined region of said substrate without irradiating a second predefined region of said substrate to remove said protecting group from said oligonucleotide mols. in said first region; and (c) contacting said substrate with a first nucleotide to couple said first nucleotide to said oligonucleotide mols. in said first predefined region, said first nucleotide having a nucleotide protecting group thereon, forming a first oligonucleotide on said substrate in said first predefined region that is different from an oligonucleotide in said second predefined region. Thus, e.g., successive coupling/deprotection sequences made use of NVOC-Leu-HOBT ester (NVOC = 6-nitroveratryloxycarbonyl, HOBT = 1-hydroxybenzotriazole), NVOC-Phe-HOBT, NVOC-Gly-HOBT, and NVOC-Gly-HOBT; the **surface** was then illuminated through a 50 .mu.m checkerboard pattern and Na-tBOC-O-t-butyl-L-Tyr was added; the entire **surface** was then uniformly irradiated to remove the remaining NVOC groups, and finally NVOC-L-Pro-HOBT was added, the NVOC group was removed by illumination, and the t-BOC and t-Bu groups were removed with TFA; the **surface** thus consisted of a 50 .mu.m checkerboard array of Tyr-Gly-Gly-Phe-Leu (I) and Pro-Gly-Gly-Phe-Leu (II). The **surface** was then exposed to mouse monoclonal antibody against .beta.-endorphin (3E7) (which binds to I but not II) followed by a second incubation with fluoresceinated goat anti-mouse for labeling the regions that bound 3E7; the resulting alternating bright and dark 50 .mu.m squares (viewed with an epi-fluorescence microscope) showed that (a) I and II were synthesized in alternate 50 .mu.m squares, (b) I attached to the **surface** is accessible for binding to antibody 3E7, and (c) antibody 3E7 does not bind to II.

L23 ANSWER 30 OF 35 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1994:676175 HCAPLUS
DOCUMENT NUMBER: 121:276175
TITLE: Light emission- or absorbance-based binding assays
INVENTOR(S): Kidwell, David A.
PATENT ASSIGNEE(S): United States Dept. of the Navy, USA
SOURCE: U.S., 20 pp.

CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5314802	A	19940524	US 1992-865526	19920409
US 5332659	A	19940726	US 1993-4009	19930115
US 5466578	A	19951114	US 1994-280537	19940726

PRIORITY APPLN. INFO.: US 1992-865526 19920409
US 1993-4009 19930115

AB A substance having binding sites for at least two mols. may be detected within a sample. A mol. which can be recognized by the substance is labeled such that when at least two of the labeled mols. are bound to binding sites on the substance, the labels on the mols. electronically interact with each other and vary the wavelength dependence of their spectra. This variation in the spectra of the label can be detected. If the sample is suspected of contg. the unlabeled form of a mol., such as biotin or cocaine, a known amt. of the above substance, along with a known amt. of the corresponding labeled biotin or cocaine is added to the sample. In this instance, the amt. of the suspect mol. in the sample is then detd. by the extent to which the variation in the spectra of the label has been reduced. Alternatively, the present invention can be used to det. the binding characteristics of the substance within the sample. The method of the present invention is useful in immunoassays or other bioassays as well as in studies of **surface** interactions. Pyrene butyric acid was **conjugated** to **PEG** and benzoylecgonine and the pyrene-labeled cocaine deriv. was tested with monoclonal antibodies and cocaine with an excitation wavelength of 343 nm and emission scanning at 350-600 nm. The ratio of emitted light at 400 nm to 378 and 396 nm was inversely proportional to the cocaine concn. Prepn. of a pyrene **linker** including biotin and its use are described as well as a computer program to simulate a binding assay.

L23 ANSWER 31 OF 35 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1994:477743 HCAPLUS
DOCUMENT NUMBER: 121:77743
TITLE: Sensor membranes containing ionophores for ion selective electrodes and biosensors and their preparation and use in the detection of analytes
INVENTOR(S): Raguse, Burkhard; Cornell, Bruce Andrew; Braach-Maksvytis, Vijoleta Lucija Bronislava; Pace, Ronald John
PATENT ASSIGNEE(S): Australian Membrane and Biotechnology Research Institute, Australia; University of Sydney
SOURCE: PCT Int. Appl., 70 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9407593	A1	19940414	WO 1993-AU509	19931001

W: AT, AU, BB, BG, BR, BY, CA, CH, CZ, DE, DK, ES, FI, GB, HU, JP, KP, KR, KZ, LK, LU, LV, MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SK, UA, US, VN
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG

EP 670751	A1	19950913	EP 1993-922449	19931001	
EP 670751	B1	20011212			
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE					
JP 08505123	T2	19960604	JP 1993-508531	19931001	
AU 672638	B2	19961010	AU 1993-51444	19931001	
AU 9351444	A1	19940426			
EP 1104883	A2	20010606	EP 2001-105279	19931001	
EP 1104883	A3	20010718			
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE					
EP 1106998	A2	20010613	EP 2001-105278	19931001	
EP 1106998	A3	20010718			
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE					
EP 1130386	A1	20010905	EP 2001-105275	19931001	
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE					
EP 1130387	A1	20010905	EP 2001-105276	19931001	
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE					
EP 1130388	A1	20010905	EP 2001-105277	19931001	
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE					
AT 210731	E	20011215	AT 1993-922449	19931001	
ES 2169725	T3	20020716	ES 1993-922449	19931001	
US 5637201	A	19970610	US 1995-406853	19950517	
US 5741409	A	19980421	US 1997-833786	19970409	
US 5753093	A	19980519	US 1997-833782	19970409	
US 5783054	A	19980721	US 1997-826903	19970409	
US 5798030	A	19980825	US 1997-826904	19970409	

PRIORITY APPLN. INFO.:

AU 1992-5069	A	19921001
AU 1993-9863	A	19930708
EP 1993-922449	A3	19931001
WO 1993-AU509	W	19931001
US 1995-406853	A3	19950517

AB The present invention relates to electrode membrane combinations for use in ion selective electrodes and biosensors. In addn., the present invention relates to methods for the prodn. of such electrode membrane combinations and the use of ion selective electrodes and biosensors incorporating such electrode membrane combinations in the detection of analytes. The present invention also relates to novel compds. used in the electrode membrane combinations. These novel compds. include a linker lipid for use in attaching a membrane including a plurality of ionophores to an electrode and providing a space between the membrane, the electrode being either in part or totally made up of the linker lipid. The linker lipid comprises within the same mol. a hydrophobic region capable of spanning the membrane, an attachment group used to attach the mol. to an electrode **surface**, a hydrophilic region between the hydrophobic region and the attachment group, and a polar head group region attached to the hydrophobic region at a site remote from the hydrophilic region. A **Au** on glass electrode was immersed in a soln. of 23-(20'-oxo-19'-oxaeicosa-(Z)-9'-ene)-70-phenyl-20,25,28,42,45-pentaoxo-24-aza-19,29,32,35,38,41,46,47,52,55-decaoxa-58,59-dithioahexaconta-(Z)-9-ene linker lipid and bis(2-hydroxyethyl)disulfide, the disulfide was allowed to adsorb, and the electrode was rinsed, dried, and clamped in a containment vessel. A soln. contg. glycerol monooleate, nonactin (ionophore), and tetradecane was added to the electrode, the electrode was

rinsed with saline soln., and urease was nonspecifically bound to the lipid membrane **surface**. On the addn. of urea, the impedance of the urease/ion selective electrode dropped more than that of the control (identical electrode lacking urease). Synthesis of membrane spanning lipids is described.

L23 ANSWER 32 OF 35 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1994:428589 HCAPLUS
DOCUMENT NUMBER: 121:28589
TITLE: Derivatized organic **solid** support for nucleic acid synthesis
INVENTOR(S): Reddy, Parameswara M.; Michael, Maged A.
PATENT ASSIGNEE(S): Beckman Instruments, Inc., USA
SOURCE: PCT Int. Appl., 131 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9401446	A2	19940120	WO 1993-US6214	19930629
WO 9401446	A3	19940303		

W: JP
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE
PRIORITY APPLN. INFO.: US 1992-910223 19920709
AB Novel particulate supports useful for **solid**-phase oligonucleotide synthesis are based on a porous polymer based on a substituted acrylate or methacrylate moieties with a nucleoside linked to it by a spacer arm .gtoreq.3 C atoms long. The **linker** can be a substituted aliph. diamine and may include a **polyethylene glycol** moiety. Preferably, the porous polymer is a methacrylate-vinylidene polymer. The **solid**-phase support can be used for oligodeoxyribonucleotide synthesis by either the phosphite-triester or the phosphotriester processes. Fractogel.RTM.-65F 10 g in dry acetonitrile 100 mL was incubated with carbonyldiimidazole 16.2 g at room temp. for 4 h and after washing with acetonitrile and drying, the crosslinked material was resuspended in dichloromethane 100 mL. The resuspended material was incubated with 1,12-diaminodecane 20 g at room temp. overnight and unreacted groups blocked with isopropylamine before washing and drying to give beads with an amino group content of 300-400 .mu.mole/g. The support was then coupled with 5'-dimethoxytrityl succinates of nucleosides to give 28.1-36.50 .mu.mole nucleoside/g. These supports were used succesfully for the synthesis of oligonucleotides in com. oligonucleotide synthesizers.

L23 ANSWER 33 OF 35 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1994:212037 HCAPLUS
DOCUMENT NUMBER: 120:212037
TITLE: Immobilization of biomolecules on perfluorocarbon **surfaces**
INVENTOR(S): Eveleigh, John W. D.
PATENT ASSIGNEE(S): du Pont de Nemours, E. I., and Co., USA
SOURCE: U.S., 8 pp. Cont.-in-part of U.S. Ser. No. 428,154, abandoned.
CODEN: USXXAM

DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5270193	A	19931214	US 1991-785887	19911024

PRIORITY APPLN. INFO.: US 1989-428154 19891027

AB A ligand or ligand receptor is securely but reversibly attached to a perfluorocarbon carrier with a water-sol. polymer, a perfluorocarbon anchoring group, and optionally a **linker**. For example, the biomol. is covalently attached to the polymer, followed by covalently attaching the anchoring group and attaching the product to the carrier. Alternatively, the anchoring group is covalently attached to the polymer, followed by attachment of the product to the carrier and then covalently attaching a biomol. to the polymer. The polymer may be starch, dextran, agarose, **PEG**, or poly(vinyl alc.). The immobilized ligand or receptor is useful in affinity sepns. and immunoassays. Thus, the triazine dye, Procion Red H-3B, was **conjugated** with poly(vinyl alc.) in aq. soln., and the **conjugate** was acylated with pentafluorobenzoyl chloride and adsorbed onto a Perflex 35S **solid** perfluorocarbon chromatog. carrier. A column packed with the dye-bearing carrier was used for chromatog. purifn. of crude muscle lactate dehydrogenase (purifn. factor 4.8, recovery 71%).

L23 ANSWER 34 OF 35 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1994:129086 HCAPLUS
DOCUMENT NUMBER: 120:129086
TITLE: Self-assembling reagent monolayer with short-chained linker
INVENTOR(S): Guder, Hans Joachim; Klein, Christian; Liley, Martha; Spinke, Juergen; Knoll, Wolfgang
PATENT ASSIGNEE(S): Boehringer Mannheim G.m.b.H., Germany
SOURCE: Eur. Pat. Appl., 22 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

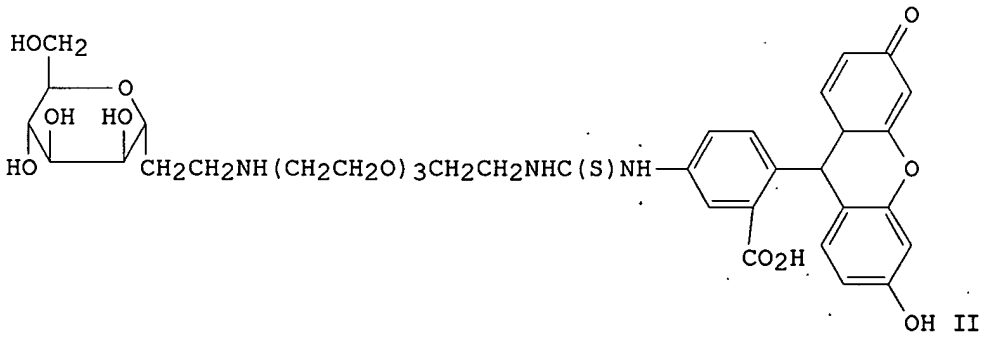
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 574000	A1	19931215	EP 1993-109319	19930609
EP 574000	B1	19970827		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
DE 4039677	A1	19920617	DE 1990-4039677	19901212
WO 9210757	A1	19920625	WO 1991-EP2393	19911212
W: JP, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, MC, NL, SE				
EP 515615	A1	19921202	EP 1992-900474	19911212
EP 515615	B1	19960904		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE				
JP 05502515	T2	19930428	JP 1992-502451	19911212
JP 3071823	B2	20000731		
AT 142340	E	19960915	AT 1992-900474	19911212
ES 2093813	T3	19970101	ES 1992-900474	19911212

DE 4219159	A1	19931216	DE 1992-4219159	19920611
AT 157458	E	19970915	AT 1993-109319	19930609
ES 2108781	T3	19980101	ES 1993-109319	19930609
JP 06082455	A2	19940322	JP 1993-140627	19930611
US 5763191	A	19980609	US 1994-279715	19940725

PRIORITY APPLN. INFO.:
DE 1990-4039677 A 19901212
DE 1992-4219159 A 19920611
WO 1991-EP2393 W 19911212
US 1992-928915 B1 19920812

AB A reagent for specific binding reactions is immobilized on a **solid** carrier as a dil., laterally homogeneous monolayer from an aq. soln. contg. the reagent, linked via a short-chain spacer mol. to an anchoring group, and .gtoreq.1 hydrophilic diluent without use of solubilizers such as detergents. Preferred diluents are X1SSX2 and X3SH [X1-X3 = (CH2)nC(O)NHLY; n = 1-6; L = hydrophilic linker group; Y = hydrophilic end group, e.g. NH2, OH, CO2H, SO3H]. Thus, a chromed prism in Kretschmann configuration, coated with **Au** by vapor deposition, was used for immobilization of bisbiotinoylcystamine (I). Streptavidin binding to the biotinylated **surface**, measured by laser reflectance using Fresnel's equations, was optimized by diln. of I with HSCH2CH2C(O)NHCH2CH2OCH2CH2OH. I was prepd. by reaction of biotin N-hydroxysuccinimide ester with cystaminium dichloride.

L23 ANSWER 35 OF 35 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1991:429746 HCAPLUS
DOCUMENT NUMBER: 115:29746
TITLE: The synthesis of heterobifunctional linkers for the **conjugation** of ligands to molecular probes
AUTHOR(S): Bertozzi, Carolyn R.; Bednarski, Mark D.
CORPORATE SOURCE: Dep. Chem., Univ. California, Berkeley, CA, 94720, USA
SOURCE: Journal of Organic Chemistry (1991), 56(13), 4326-9
CODEN: JOCEAH; ISSN: 0022-3263
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 115:29746
GI



II

AB The heterobifunctional **polyethylene glycol linker** H2N(CH2CH2O)3CH2CH2N3 (I) was synthesized. This **linker** contains a free amine that can be **conjugated** directly to biol. mols. or probes and an azide that can be reduced to an

amine for **conjugation** to other mols. As an example of the use of I, a carbohydrate-fluorescein **conjugate** II was synthesized for use in cell-**surface** receptor studies.